Astroglial cells regulate the developmental timeline of human neurons differentiated from induced pluripotent stem cells.

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Public Summary:
In this work, we show that human iPSC-derived neurons cultivated in the presence of astrocytes mature faster than neurons without. We performed several morphological and electrophsyoloigcal experiments to prove that the presence of astrocytes are essential for neurons to form connections (synapses) and communicate with each other. In conclusion, we demonstrated the positive effects of astrocytes and showed a new protocol to speed up neuronal maturation. This would likely be useful for follow up experiments on disease modeling and drug screening.

Scientific Abstract:
Neurons derived from human induced-pluripotent stem cells (hiPSCs) have been used to model a variety of neurological disorders. Different protocols have been used to differentiate hiPSCs into neurons, but their functional maturation process has varied greatly among different studies. Here, we demonstrate that laminin, a commonly used substrate for iPSC cultures, was inefficient to promote fully functional maturation of hiPSC-derived neurons. In contrast, astroglial substrate greatly accelerated neurodevelopmental processes of hiPSC-derived neurons. We have monitored the neural differentiation and maturation process for up to two months after plating hiPSC-derived neuroprogenitor cells (hNPCs) on laminin or astrocytes. We found that one week after plating hNPCs, there were 21-fold more newly differentiated neurons on astrocytes than on laminin. Two weeks after plating hNPCs, there were 12-fold more dendritic branches in neurons cultured on astrocytes than on laminin. Six weeks after plating hNPCs, the Na(+) and K(+) currents, as well as glutamate and GABA receptor currents, were 3-fold larger in neurons cultured on astrocytes than on laminin. And two months after plating hNPCs, the spontaneous synaptic events were 8-fold more in neurons cultured on astrocytes than on laminin. These results highlight a critical role of astrocytes in promoting neural differentiation and functional maturation of human neurons derived from hiPSCs. Moreover, our data presents a thorough developmental timeline of hiPSC-derived neurons in culture, providing important benchmarks for future studies on disease modeling and drug screening.